At page 1, please replace the last paragraph flowing to page 2 with the following:

--Diagnosis of factor VIII inhibitors is commonly performed using the so-called Bethesda assay (Kasper et al. 1975, Thromb. Diath. Haemorrh. 34: 869-872). In this assay equal amounts of normal plasma and dilutions of inhibitor plasma are incubated for two hours at 37°C. Next, residual factor VIII activity is determined and compared to control incubation in which normal plasma is incubated with 0.1 M imidazole for 2 hours at 37°C. The amount of inhibitor is expressed in Bethesda units; one Bethesda unit corresponds to the amount of inhibitor that is capable of reducing the activity of factor VIII in normal plasma by 50%. A recent study has proposed several adaptations to the original assay system which serve to improve the stability of factor VIII during the assay (Verbruggen et al. 1995, Thromb. Haemostas. 73: 247-251). This so-called "Nijmegen modification" of the Bethesda assay is particularly useful for the detection of low titre factor VIII inhibitors. It should be noted that the Bethesda assay does not provide information on the epitopes of factor VIII inhibitory antibodies.--

At page 2, please replace the last paragraph flowing to page 3 with the following:

--An alternative treatment of patients with factor VIII inhibitor constitutes the use of factor VIII bypassing agents. Activated prothrombin concentrate complexes (APCC) have been used to bypass the activity of factor VIII. APCC has been used successfully to control bleeding episodes in a large number of patients with an inhibitor. However, treatment is not effective in all cases and an anamnestic rise in

the titre of the inhibitor following administration of APCC (most likely due to trace amounts of factor VIII in the preparation) has been reported in a number of patients. In the last 5 years recombinant factor VIIa has become available as a new factor VIII bypassing agent for the treatment of patients with an inhibitor (Lusher et al. 1996. Haemostasis 26 (suppl. 1): 124-130). Recombinant factor VIIa has been successfully used to control the bleeding episodes in patients with an inhibitor. Treatment by this agent is however limited by the short half-life of this compound in the circulation which requires multiple infusions at relatively short time intervals. APC-resistant factor V has recently been suggested as an alternative means to bypass the biological activity of factor VIII inhibitors (WO 95/29259). The agents described above do not act directly on factor VIII inhibitors but merely serve to bypass factor VIII by infusion of large amounts of clotting factor concentrates with increased procoagulant activity.

At page 3, please replace the last paragraph flowing to page 4 with the following:

--This invention relates to methods for diagnosis and treatment using inhibitory antibodies directed against factor VIII. Methods are disclosed that show how to arrive at nucleotide and amino acid sequences that encode factor VIII specific antibodies. This invention discloses diagnostic tests that allow for detection of nucleotide and amino acid sequences that encode factor VIII specific antibodies within a heterogeneous mixture of antibody-encoding nucleotide or amino acid sequences. This invention further discloses how to use recombinant antibody fragments which bind specifically to factor VIII as novel therapeutic agents for the treatment of patients with factor VIII inhibitors.--